

**Amendments to the Claims:**

Please replace paragraph [0001] with the following amended paragraph:

[0001] The present application is a continuation of application Serial No. 09/893,348 filed June 28, 2001, now abandoned, itself a continuation-in-part of application Serial No. 09/314,161, filed May 19, 1999, now abandoned, which is a continuation-in-part of application No. PCT/US98/14715, filed July 21, 1998, and is a continuation-in-part of application Serial No. 09/218,277, filed December 22, 1998, now abandoned, the entire contents of each of which are hereby incorporated herein by reference.

Please replace paragraph [0011] with the following amended paragraph:

[0011] The parent applications, application nos. 09/218,277, now abandoned, and 09/314,161, now abandoned, and PCT Publication WO 99/60021, describe the discovery made in the laboratory of the present inventors that activated T cells that recognize an antigen of the NS of the patient confer neuroprotection. More specifically, T cells reactive to MBP were shown to be neuroprotective in rat models of partially crushed optic nerve (see also Moalem et al, 1999a, the entire contents of which being hereby incorporated herein by reference) and of spinal cord injury (see also Hauben et al, 2000, the entire contents of which being hereby incorporated herein by reference). Until recently, it had been thought that immune cells do not participate in NS repair.

Furthermore, any immune activity in the context of CNS damage was traditionally considered detrimental for recovery. It was quite surprising to discover that NS-specific activated T cells could be used to protect nervous system tissue from secondary degeneration which may follow damage caused by injury or disease of the CNS or PNS. The mechanism of action of such NS-specific T cells has yet to be discovered, but the massive accumulation of exogenously administered T cells at the site of CNS injury suggests that the presence of T cells at the site of injury plays a prominent role in neuroprotection. It appears, however, that the accumulation, though a necessary condition, is not sufficient for the purpose, as T cells specific to the non-self antigen ovalbumin also accumulate at the site, but have no neuroprotective effect (Hirschberg et al, 1998).

Amendments to the Claims:

This listing of the claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (Currently Amended). A method for reducing secondary neuronal degeneration that follows neuronal damage caused by an injury, disease, disorder or condition caused by the neurodegenerative effects of disease, or for reducing secondary neuronal degeneration that follows the primary neuronal damage of an injury, in the central or peripheral nervous system of an individual in need thereof, comprising:

causing T cells activated against a nervous system (NS)-specific antigen which, in its native state, is present at the site of secondary neuronal degeneration, to accumulate at the site of secondary neuronal degeneration in the individual in need, thereby reducing secondary neuronal degeneration at that site, wherein, when the individual in need has an autoimmune disease, the NS-specific antigen is not the autoimmune antigen of that disease, and when the individual in need has a neoplasm, the NS-specific antigen is one that does not appear in the neoplasm-,

wherein said causing step is accomplished by - administering an effective amount of (i) said NS-specific antigen, (ii) an immunogenic or cryptic epitope thereof, or (iii) a modification of (i) that is immunogenic but not encephalitogenic, in such a manner as to cause a T cell response thereto, such that T cells become activated

against the NS-specific antigen which is present at the site of secondary neuronal degeneration; or

administering an effective amount of T cells that are activated against said NS-specific antigen, said immunogenic or cryptic epitope thereof, or said modification thereof.

2 (Currently Amended). A method in accordance with claim 1, wherein said activated T cells are caused to accumulate at the site of secondary neuronal degeneration by administering an effective amount of said NS-specific antigen, ~~or an said~~ immunogenic or cryptic epitope thereof, or said modification thereof, in such a manner as to cause a T cell response thereto, such that T cells become activated against the NS-specific antigen which is present at the site of secondary neuronal degeneration.

3 (Currently Amended). A method in accordance with claim 1, wherein said activated T cells are caused to accumulate at the site of secondary neuronal degeneration by administering an effective amount of T cells that are activated against said NS-specific antigen, said immunogenic or cryptic epitope thereof, or said modification thereof.

4. (Original). A method in accordance with claim 3, wherein said T cells are autologous.

5. (Original). A method in accordance with claim 1, wherein the individual in need is one suffering from an injury that has caused primary neuronal damage.

6 (Canceled).

7 (Currently Amended). A method in accordance with claim 1, wherein the individual in need is one suffering from a disease, disorder or condition that has neurodegenerative effects.

8 (Canceled).

9 (Currently Amended). A method for ameliorating the secondary neurodegenerative effects of an injury-~~or~~, disease, disorder or condition that causes secondary neuronal degeneration of the central or peripheral nervous system of an individual in need thereof, comprising:

causing T cells activated against a nervous system (NS)-specific antigen which, in its native state, is present at the site of secondary neuronal degeneration, to accumulate at the site of secondary neuronal degeneration in the individual in need, thereby ameliorating the effects of the injury, ~~or~~ disease, condition or disorder at that site, wherein, when the individual in need has an autoimmune disease, the NS-specific antigen is not the autoimmune antigen of that disease, and when the individual in need has a neoplasm, the NS-specific antigen is one that does not appear in the neoplasm-~~,~~

wherein said causing step is accomplished by -  
administering an effective amount of (i) said NS-specific antigen, (ii) an immunogenic or cryptic epitope thereof, or (iii) a modification of (i) that is immunogenic but not encephalitogenic, in such a manner as to cause a T cell response thereto, such that T cells become activated

against the NS-specific antigen which is present at the site of secondary neuronal degeneration; or

administering an effective amount of T cells that are activated against said NS-specific antigen, said immunogenic or cryptic epitope thereof, or said modification thereof.

10 (Currently Amended). A method in accordance with claim 9, wherein said activated T cells are caused to accumulate at the site of secondary neuronal degeneration by administering an effective amount of said NS-specific antigen, ~~or an~~ said immunogenic or cryptic epitope thereof, or said modification thereof, in such a manner as to cause a T cell response thereto, such that T cells become activated against the NS-specific antigen which is present at the site of secondary neuronal degeneration.

11 (Currently Amended). A method in accordance with claim 9, wherein said activated T cells are caused to accumulate at the site of secondary neuronal degeneration by administering an effective amount of T cells that are activated against said NS-specific antigen, said immunogenic or cryptic epitope thereof, or said modification thereof.

12 (Original). A method in accordance with claim 11, wherein said T cells are autologous.

13 (Original). A method in accordance with claim 9, wherein the individual in need is one suffering from an injury that has caused primary neuronal damage.

14 (Canceled).

15 (Original). A method in accordance with claim 9, wherein the individual in need is one suffering from a disease, condition or disorder that has neurodegenerative effects.

16 (Canceled).

17 (New). The method according to claim 3, wherein said T cells are semi-allogeneic T cells.

18 (New). The method according to claim 3, wherein said activated T cells have been sensitized to said NS-specific antigen, said immunogenic or cryptic epitope thereof, or said modification thereof.

19 (New). The method according to claim 3, wherein the NS-specific antigen is selected from the group consisting of myelin basic protein (MBP), myelin oligodendrocyte glycoprotein (MOG), proteolipid protein (PLP), myelin-associated glycoprotein (MAG), S-100,  $\beta$ -amyloid, Thy-1, P0, P2, and a neurotransmitter receptor.

20 (New). The method according to claim 19, wherein the NS-specific antigen is MBP.

21 (New). The method according to claim 19, wherein the NS-specific antigen is selected from the group consisting of Nogo-A, Nogo-B, Nogo-C, and Nogo receptor.

22 (New). The method according to claim 18, wherein activated T cells have been sensitized to an immunogenic epitope or a cryptic epitope of said NS-specific antigen.

23 (New). The method according to claim 22, wherein said an immunogenic epitope or cryptic epitope is one derived from MBP.

24 (New). The method according to claim 23, wherein said activated T cells have been sensitized to a peptide selected from the group of sequences consisting of the sequences p11-30, p51-70, p87-99, p91-110, p131-150, and p151-170 of MBP.

25 (New). The method according to claim 24, wherein said peptide corresponds to the sequence p51-70 of MBP.

26 (New). The method according to claim 22, wherein said immunogenic epitope or cryptic epitope is one derived from MOG.

27 (New). The method according to claim 26, wherein said activated T cells have been sensitized to the sequence p35-55 of MOG.

28 (New). The method according to claim 22, wherein said immunogenic epitope or cryptic epitope is one derived from Nogo.

29 (New). The method according to claim 28, wherein said activated T cells have been sensitized to the Nogo-A p472 peptide (SEQ ID NO:19).

30 (New). The method according to claim 22, wherein said immunogenic epitope or cryptic epitope is one derived from Nogo receptor.

31 (New). The method according to claim 4, wherein said autologous T cells have been stored for future use.



32 (New). The method according to claim 2, wherein the NS-specific antigen is selected from the group consisting of myelin basic protein (MBP), myelin oligodendrocyte glycoprotein (MOG), proteolipid protein (PLP), myelin-associated glycoprotein (MAG), S-100,  $\beta$ -amyloid, Thy-1, P0, P2, and a neurotransmitter receptor.

33 (New). The method according to claim 32, wherein the NS-specific antigen is MBP.

34 (New). The method according to claim 33, wherein the MBP is administered orally.

35 (New). The method according to claim 2, wherein the NS-specific antigen is selected from the group consisting of Nogo-A, Nogo-B, Nogo-C, and Nogo receptor.

36 (New). The method according to claim 2, wherein said NS-specific antigen, immunogenic or cryptic epitope thereof, or modification thereof, is an immunogenic or cryptic epitope of said NS-specific antigen.

37 (New). The method according to claim 36, wherein said immunogenic or cryptic epitope is one derived from MBP.

38 (New). The method according to claim 37, wherein said immunogenic or cryptic epitope is a peptide selected from the sequences consisting of the sequences p11-30, p51-70, p87-99, p91-110, p131-150, and p151-170 of MBP.

39 (New). The method according to claim 38, wherein said peptide corresponds to the sequence p51-70 of MBP.

40 (New). The method according to claim 36, wherein said immunogenic or cryptic epitope is one derived from MOG.

41 (New). The method according to claim 40, wherein said immunogenic or cryptic epitope is a peptide with the sequence p35-55 of MOG.

42 (New). The method according to claim 36, wherein said immunogenic or cryptic epitope is one derived from Nogo.

43 (New). The method according to claim 42, wherein said immunogenic or cryptic epitope is the Nogo-A p472 peptide (SEQ ID NO:19).

44 (New). The method according to claim 36, wherein said immunogenic or cryptic epitope is one derived from Nogo receptor.

45 (New). The method according to claim 2, wherein said NS-specific antigen, immunogenic or cryptic epitope thereof, or modification thereof, is administered intravenously, intrathecally, intramuscularly, intradermally, topically, subcutaneously, or mucosally.

46 (New). The method according to claim 45, wherein said mucosal administration is selected from the group consisting of oral, intranasal, buccal, vaginal and rectal administration.

47 (New). The method according to claim 46, wherein said NS-specific antigen, immunogenic or cryptic epitope thereof, or modification thereof, is administered orally and the individual is actively immunized to build up a critical T cell response.

48 (New). The method according to claim 5, wherein said injury is spinal cord injury.

49 (New). The method according to claim 13, wherein said injury is spinal cord injury.

50 (New). A method in accordance with claim 1, wherein said modification of (i) that is immunogenic but not encephalitogenic is a modification that consists of the replacement of one or more amino acid residues of (i) by different amino acid residues at the T-cell receptor binding site, said modification of (i) still being capable of recognizing the T-cell receptor recognized by the NS-specific antigen of (i), but the modification of (i) being less encephalitogenic than (i).

51 (New). A method in accordance with claim 9, wherein said modification of (i) that is immunogenic but not encephalitogenic is a modification that consists of the replacement of one or more amino acid residues of (i) by different amino acid residues at the T-cell receptor binding site, said modification of (i) still being capable of recognizing the T-cell receptor recognized by the NS-specific antigen of (i), but the modification of (i) being less encephalitogenic than (i).